Remarks

In the Specification

The Examiner alleges that the recitation in claims 8 and 22 that the concentration of ricinoleic acid is at least 90% lacks antecedent support in the disclosure. The specification has been amended to describe this embodiment as requested by the Examiner.

In the Claims

Claims 6 and 7 have been amended to correct typographical and grammatical errors. New claim 25 has been added. Support for new claim 25 is found at least at page 13, lines 21-24.

In the event this amendment and response does not overcome the Examiner's objections, the undersigned requests a telephonic interview with Examiner Fubara and her supervisor, SPE Hartley.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 6, 7, and 15-24 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Legal Standard

In reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph, by providing clear warning to others as to what constitutes infringement of the patent.

See, e.g., *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379, 55 USPQ2d 1279, 1283 (Fed. Cir. 2000). See also *In re Larsen*, No. 01-1092 (Fed. Cir. May 9, 2001) (unpublished). See also *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1366, 71 USPQ2d 1081, 1089 (Fed. Cir. 2004) ("The requirement to 'distinctly' claim means that the claim must have a meaning discernible to one of ordinary skill in the art when construed according to correct principles....Only when a claim remains insolubly ambiguous without a discernible meaning after all reasonable attempts at construction must a court declare it indefinite.").

Accordingly, a claim term that is not used or defined in the specification is not indefinite if the meaning of the claim term is discernible. *Bancorp Services, L.L.C. v. Hartford Life Ins. Co.*, 359 F.3d 1367, 1372, 69 USPQ2d 1996, 1999-2000 (Fed. Cir. 2004) (holding that the disputed claim term "surrender value protected investment credits" which was not defined or used in the specification was discernible and hence not indefinite because "the components of the term have well recognized meanings, which allow the reader to infer the meaning of the entire phrase with reasonable confidence").

Analysis

The Examiner alleges that claims 6 and 15 are indefinite because the boundaries of the term "ester derivatives" are not clearly defined. Application respectfully disagrees. Claim 15 has been amended to delete the phrase "a derivative thereof". Therefore, the Examiner's rejection is moot.

Claim 6 depends from claim 1 and specifies that the poly(ester-anhydride) comprises one or more monomers derived from, among others, non-linear fatty acid-ester derivatives of

ricinoleic acid. The specification discloses examples of non-linear fatty acid-ester derivatives of ricinoleic acid, such as alkyl O-esters and carbonates of ricinoleic acid and oligo(hydroalkanoic acid)-O-esters and carbonates of ricinoleic acid (page 14, lines 10-13); hydroxyl-acid terminated oligomers containing a ricinoleic acid terminal, such as poly(lactic acid)-terminated oligomers containing a ricinoleic acid terminal (page 14, lines 24-28); ricinoleic acid methyl ester (page 20, Example 1, Method 1); and ricinoleic acid stearyl ester, myristoyl ester, lauryl ester, octanoyl ester, and ricinoleic acid-oligo lactide ester (pages 23-26, Example 2). One of ordinary skill in the art would understand the term "non-linear fatty acid-ester derivatives of ricinoleic acid", particularly when read in light of the specification. Accordingly, claim 6 is definite.

Rejection Under 35 U.S.C. § 102/§ 103

Claims 15-21 and 24 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,473,103 to Domb *et al.* ("Domb"). Claims 1 and 8 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,756,652 to Storey *et al.* ("Storey"). Claims 1-8 and 10 were rejected under 35 U.S.C. § 102(b) as being anticipated by, or in the alternative under 35 U.S.C. § 103(a) as obvious over Teomim *et al., J. Biomed. Mat. Res.*, Vol. 45, Issue 3, pp. 258-27 (1999) ("Teomim") or Domb *et al., Acta. Polym.*, Vol. 49, Issue 10-11, pp. 526-533 (1988) ("Domb 2"). Applicants respectfully traverse this rejection.

Legal Standard

For a rejection of claims to be properly founded under 35 U.S.C. § 102, it must be established that a prior art reference discloses each and every element of the claims. *Hybritech Inc. v Monoclonal Antibodies Inc.*, 231 USPQ 81 (Fed. Cir. 1986), cert. denied, 480 US 947

(1987); *Scripps Clinic & Research Found v. Genentech Inc.*, 18 USPQ2d 1001 (Fed. Cir. 1991). The Federal Circuit held in Scripps, 18 USPQ2d at 1010:

> Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. . . *There must be no difference* between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. (Emphasis added)

A reference that fails to disclose even one limitation will not be found to anticipate, even if the missing limitation could be discoverable through further experimentation. As the Federal Circuit held in Scripps, Id.:

> [A] finding of anticipation requires that all aspects of the claimed invention were already described in a single reference: a finding that is not supportable if it is necessary to prove facts beyond those disclosed in the reference in order to meet the claim limitations. The role of extrinsic evidence is to educate the decision-maker to what the reference meant to persons of ordinary skill in the field of the invention, not to fill in the gaps in the reference.

For a prior art reference to anticipate a claim, it must enable a person skilled in the art to practice the invention. The Federal Circuit held that "a §102(b) reference must sufficiently describe the claimed invention to have placed the public in possession of it. . . [E]ven if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it was not enabling." *Paperless Accounting Inc v Bay Area Rapid Transit Sys.*, 231 USPQ 649, 653 (Fed. Cir. 1986).

Analysis

Domb

Domb describes monomeric diacid derivatives that contain at least two fatty acids coupled by a hydrolytically or enzymatically degradable bond (abstract). The hydrolytically or enzymatically degradable bond can be cleaved to form monomers, which can be polymerized. Contrary to the Examiner's assertion, the polymers in Figure 2 are polyanhydrides, not poly(ester anhydrides) as required by claims 15-21 and 24. Figure 2 shows the release profile of ciprofloxacin from ricinoleic acid maleate-based polymeric devices (col. 2, lines 60-63). All of the polymers in Figure 2 are polyanhydrides; the linkage between monomer units is an anhydride bond, not a combination of anhydride bonds and random ester bonds as required by the claims (see the legend in Figure 1). Domb does not disclose each and every element of claims 15-21 and 24. Accordingly, claims 15-21 and 24 are novel over Domb.

Storey

Storey describes biodegradable poly(ester-anhydrides) (abstract). Storey discloses that the polyester segment components can contain a homopolymer, copolymer, or terpolymer of biocompatible hydroxy acids, for example, lactic acid, glycolic acid, ε-hydroxycaproic acid and γ-hydroxyvaleric acid (col. 3, lines 27-31). Alternatively, Storey discloses, the polyester segments can be formed by copolymerization of a polyhydric alcohol and a biocompatible polycarboxylic acid (col. 3, lines 31-33). Storey discloses that most typically, such copolymers are formed between dihydric alcohols, for example, propylene glycol, and biocompatible dicarboxylic acids (col. 3, lines 33-36).

Storey does not disclose or suggest biodegradable poly(ester anhydrides) having random ester bonds in the polymer backbone. As shown in Figures 1 and 6, the ester linkages occur at regular intervals in the polyester blocks, and thus are not randomly situated along the polymer backbone between monomers units or blocks as required by the claims 1 and 8.

The Examiner alleges that Storey does not exclude the ester moiety from being random so that randomness of the ester bond would be inherent. This is not the standard for inherency.

"To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted).

"In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original)

The Examiner alleges that random ester bonds are inherent in the polymers described in Storey. However, the Examiner has provided no basis in fact and/or technical reasoning to reasonably support such an allegation as required under the doctrine of inherency. The Examiner alleges that burden is on the applicant to factually show that the ester bonds in Storey are not random. However, the burden shifts to the applicant only after the Examiner has established that

the claimed polymers are substantially identical to the polymers described in Storey (MPEP 2112(V)). The Examiner has provided no analysis of the structures of the polymers described in Storey, nor methods of making thereof, to support the allegation that the polymers in Storey are substantially identical to the claimed polymers.

The Examiner also alleges that in response to Applicant's arguments that the ester bonds in the polymers in Figure 1 and 6 are at regular intervals, applicant has not pointed to applicant's polyester blocks having random ester bonds. Again, this is not correct legal standard for inherency. Under the doctrine of inherency, the Examiner must provide a basis in fact and/or technical reasoning showing that random ester bonds are necessarily present in the polymers in Storey, not that the claimed compositions contain the inherent feature. The Examiner has provided no such factual basis and/or technical reasoning. The fact that Storey may describe different polymerization reactions does not change the fact that all the reactions described in Storey results in polymers containing regular ester bonds.

However, contrary to the Examiner's assertion, applicants have shown that the claimed compositions contain random ester bonds in the polymer backbone. Polyanhydride prepolymers can be reacted with a polyfunctional organic molecule, such as a hydroxyl acid, to form terminally functionalized polyanhydride oligomers. Since the polyfunctional organic molecule can react anywhere along the polyanhydride polymer, the result is polyanhydride oligomers of different lengths having terminal reactive functional groups. The functionalized oligomers can be repolymerized to form a polyanhydride having ester bonds randomly distributed along the polymer backbone. Accordingly, claims 1 and 8 are novel over Storey.

Teomim

Teomim describes polyanhydrides synthesized from ricinoleic acid half-esters with maleic and succinic anhydrides (abstract). The polymers described in Teomim are polyanhydride copolymers that are formed from the melt condensation of diacids and contain only anhydride bonds between the monomer units. While there are ester bonds within the monomer units (between the malic and succinate group and the hydroxyl group of ricinoleic acid), there are no random ester bonds between monomers or oligomers in the polymer backbone as required by claims 1-8 and 10. Teomim does not disclose or suggest poly(ester-anhydrides), let alone poly(ester-anhydrides) copolymers containing random ester bonds as required by independent claim 1 and the claims dependent thereon. Accordingly, claims 1-8 and 10 are novel and non-obvious over Teomim.

Further, one of ordinary skill in the art would not be motivated to modify the polyanhydrides of Teomim to arrive at the claimed compositions. The claimed compositions contain a poly(ester-anhydride) containing random ester bonds in the polymer backbone. The polymers are typically liquids at room temperature (page 7, lines 27-30) and thus can be administered by injection. The polymers release incorporated active agents over several weeks, which is longer than solid polymers prepared from the same monomers (page 7, lines 27-30). The slower release is due to the fact that when the polymer are placed in an aqueous medium (e.g., buffer solution, or tissue or biological mediums), the viscosity of the polymer increases (page 7, line 30 to page 8, line 3). This increase in viscosity results in a semisolid compact implant that keeps it integrity while slowly degrading and releasing incorporated drug (page 8,

lines 3-6). These polymers also exhibited improved solubility compared to polyanhydrides (page 31, line 17 to page 32, line 2). The slower release of incorporated active agents and improved stability could not have been predicted from the polyanhydrides described in Teomim. Therefore, one ordinary skill in the art would not have been motivated to modify the polyanhydrides of Teomim to arrive at the claimed compositions. Accordingly, claims 1, 8, and 9 are not obvious over Teomim.

Domb 2

Domb 2 describes biopolymers for use as drug carriers and bioactive macromolecules (abstract). Domb 2 discloses that polyanhydrides synthesized from non-linear hydrophobic fatty acid esters, based on ricinoleic acid, maleic acid, and sebacic acid allegedly possess desired physicochemical properties (page 526, 2nd column, 4th paragraph, lines 8-11). These polymers are polyanhydrides (i.e., contain only anhydride bonds between monomer units), not poly(ester-anhydrides) as required by the claims.

Domb 2 also describes block copolyester-anhydrides (page 530, 1st col., 2nd paragraph). Domb 2 describes ABA-type block copolymers of poly(propylene fumarate) (PPF) and lactide (page 530, 1st col., 3rd paragraph). The ester bonds in the block copolyester-polyanhydride polymers described in Domb are between the ester monomers units in the ester block (*see* structure 4 on page 530). These ester bonds are not random between monomers, oligomers, or blocks along the polymer backbone as required by the claims. Domb 2 does not disclose each and every element of the claims. Accordingly, claims 1-8 and 10 are novel over Domb 2.

Further, one of ordinary skill in the art would not be motivated to modify the block copolyester-polyanhydrides of Domb 2 to arrive at the claimed composition. The Examiner admits that Domb 2 is silent regarding random ester bonds. However, the Examiner alleges that since Domb 2 prepares the polymers with the same reactants in the same manner as the applicants, the random ester bonds are inherent. Applicants respectfully disagree. As discussed above, the copolyester-polyanhydrides described in Domb 2 are block copolymers, wherein the ester bonds are between the monomer units in the ester block, not between anhydride blocks as in the claimed compositions. The ABA block copolymers described in Domb 2 are prepared by ring opening polymerization of lactide using stannous octoate and PPF-diol as initiator (page 530, 1st col., 3rd paragraph). In contrast, the claimed compositions can be prepared by reacting polyanhydride prepolymers with a polyfunctional organic molecule to form end-functionalized polyanhydride oligomers and then repolymerizing the oligomers to form poly(ester anhydrides) containing random ester bonds along the polymer backbone. The ABA block copolymers described in Domb 2 are structurally different from the copolymers in the claimed composition.

Alternatively, the Examiner alleges that the randomness of the ester bonds within the polymer would be obvious because the preparation method of Domb 2 does not exclude random ester bonds. Applicants respectfully disagree. As discussed above, the method of synthesis in Domb 2 clearly excludes random ester bonds. Accordingly, claims 1, 8, and 9 are not obvious over Domb 2.

Rejection Under 35 U.S.C. § 103

Claims 1, 2, 3, 9, and 10 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Storey, in view of U.S. Patent No. 5,648,096 to Gander *et al.* ("Gander") or U.S. Patent No. 5,626,862 to Brem *et al.* ("Brem"). Claims 1 and 8 rejected under 35 U.S.C. § 103(a) as being unpatentable over Teomim or Domb 2. Claims 15, 19, and 21-23 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Domb in view of O'Hagan, *Adv. Drug Del. Rev.,* 1 Dec., pp. 305-320 (1998) ("O'Hagan"). Applicants respectfully traverse this rejection.

Legal Standard

"The proper analysis under § 103, was recently reviewed by the U.S. Supreme Court in KSR International, Inc. v. Teleflex, Inc, 2007 U.S. LEXIS 4745; 75 U.S.L.W. 4289. In KSR, the Court stated:

> "If a person of ordinary skill in the art can implement a predictable variation, and would see the benefit of doing so, §103 likely bars its patentability. Moreover, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond that person's skill. A court must ask whether the improvement is more than the predictable use of prior-art elements according to their established functions. Following these principles may be difficult if the claimed subject matter involves more than the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for the improvement. To determine whether there was an apparent reason to combine the known

> elements in the way a patent claims, it will often be necessary to look to the interrelated teachings of multiple patents; to the effects of demands known to the design community or present in the marketplace; and to the background knowledge possessed by a person having ordinary skill in the art. To facilitate review, this analysis should be made explicit. But it need not seek out precise teachings directed to the challenged claim's specific subject matter, for a court can consider the inferences, and creative steps a person of ordinary skill in the art would employ."

The Federal Circuit's decisions since KSR reflect an appropriately nuanced application of TSM analysis required by KSR and Graham. *See In re Translogic Tech., Inc.*, 504 F.3d 1249, 1260 (Fed. Cir. 2007) (commenting generally on the implications of KSR for the Federal Circuit's obviousness assessments). Thus, where the claimed invention makes a routine addition of modern electronics to older devices, the Federal Circuit has found the requisite motive to make the combination in the knowledge and ordinary creativity of a person of ordinary skill. See *In re Translogic Tech.*, 504 F.3d at 1262; *Leapfrog Enters., Inc. v. Fisher-Price, Inc.*, 485 F.3d 1157, 1161 (Fed. Cir. 2007). Similarly, combinations of known options in the mechanical arts to solve the problem addressed by the claimed invention may make the invention obvious, for the person or ordinary skill would be motivated by the problem to try such combinations and achieve the same result. *In re Icon Health & Fitness, Inc.*, 496 F.3d 1374 (Fed. Cir. 2007).

In the chemical arts, where compounds are so similar as to create an expectation that the claimed new compound would have similar properties as the prior art compounds, the Federal Circuit also has upheld a finding that the claimed invention is not patentable. *Aventis Pharma*

Deutschland GmbH v. Lupin, Ltd., 499 F.3d 1293, 1301 (Fed. Cir. 2007). However, when the prior art disclosed a broad selection of compounds that might have been potential candidates for further investigation, the lack of sufficient guidance and predictability to select the compound at issue supported a finding of nonobviousness. *Takeda Chem. Indus. Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1359-60 (Fed. Cir. 2007), petition for cert. filed, 76 U.S.L.W. 3374 (U.S. Dec. 20, 2007) (No. 07-838); see also *In re Sullivan*, 498 F.3d 1345 (Fed. Cir. 2007) (remanding to the Board, noting that despite close similarity of the claimed invention and prior art, rebuttal evidence to which the Board gave inadequate consideration showed unexpected results, a teaching away from appellant's invention and a long felt but unmet need).

Where there is structural similarity between a chemical compound and prior art compounds, the court notes that, "obviousness based on structural similarity thus can be proved by identification of some motivation that would have led one of ordinary skill in the art to select and then modify a known compound (i.e., a lead compound) in a particular way to achieve the claimed compound." Slip Op. at 4 (citing *Takede Chem. Indus. v. Alpha Farm Pty., Ltd.*, supra, 492 F.3d at 1356). The Federal Circuit notes that, under KSR, what must be demonstrated is the possession of a sufficiently close relationship between the claimed and the prior art compound to create an expectation, in light of the entirety of the prior art, that the new compound will have similar properties to the old. (citing *Aventis Pharma Deutschland GmbH v. Lupin Ltd.*, supra, which relied upon *In re Dillon*, 919 F.2d 688, 692 (Fed. Cir. 1990) (en banc)). Thus, even though the prior art compound and the patented compound were virtually identical except for a substitution at a particular position on a pyridine ring, because expert testimony showed (1) there

were significant differences between compounds that achieved anti-ulcer action and compounds that inhibited gastric acid and (2) the prior art compound provided a special path to achieve certain results, the prior art did not make the claimed compound obvious. There was no discernable reason for a skilled artisan to start with this "lead" prior art compound but then to modify it in a way that would eliminate an element of it to which this advantageous property was ascribed. Thus, it would not have been obvious to try certain substitutions in the chemical structure of the prior art compound to achieve the results found in the patented compound.

Even where the prior art suggests or motivates an inventor to develop the composition or process at issue, the Federal Circuit continues to recognize that there is a critical question under 35 U.S.C. § 103 as to whether the combined teachings of the prior art "would have given rise to a reasonable expectation of success" in achieving what is claimed. *PharmaStem Therapeutics, Inc. v. ViaCell, Inc.*, 491 F.3d 1342, 1360 (Fed. Cir. 2007), petition for cert. filed, 76 U.S.L.W. 3393 (U.S. Jan. 2, 2008) (No. 07-888).

Storey in view of Gander or Brem

Storey is discussed above. Storey does not disclose or suggest a poly(ester-anhydride) containing random ester bonds along the polymer backbone as required by independent claim 1 and the claims dependent thereon.

Gander and Brem disclose microimplants, such as microparticles, microspheres, and microcapsules can be used to encapsulate and deliver drugs. Gander and Brem, alone or in combination, do not cure the deficiencies of Storey. Accordingly, claims 1-10 and 15-24 are not obvious over Storey in view of Gander or Brem.

Domb 2 or Teomim

The obviousness rejections over Domb2 or Teomim are discussed above.

Domb in view of O'Hagan

Domb is discussed above. Domb does not disclose or suggest poly(ester-anhydrides) having random ester bonds along the polymer backbone. O'Hagan describes microparticles and polymers for the mucosal delivery of vaccines (abstract). O'Hagan does not cure the deficiencies of Domb. Accordingly, claims 15, 19, and 21-23 are not obvious over Domb in view of O'Hagan.

Allowance of claims 1-10 and 15-24, as amended, and new claim 25, is respectfully solicited.

Respectfully submitted,

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